



✉ EPA/EPO/OEB
D-80298 München
☎ +49 89 23899-0
TX 523 656 epmu d
FAX +49 89 23899-4465

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Generaldirektion 2

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Strehl Schübel-Hopf & Partner
Maximilianstrasse 54
80538 München
ALLEMAGNE

Erhalten
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Strehl et al.

Telephone numbers: Branch at The Hague

Primary Examiner
(substantive examination) +31 70 340-4124

Formalities Officer / Assistant
(Formalities and other matters) +31 70 340-2667



Application No. 01 109 779.7 - 1212	Ref. EPA-53592	Date 11.06.2004
Applicant Ajinomoto Co., Inc.		

Communication pursuant to Article 96(2) EPC

Fr.: 21. Okt. 04
Btg.: 21. Sept. 04

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 36(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).



DEVIJVER K
Primary Examiner
for the Examining Division

Enclosure(s): 8 page/s reasons (Form 2906)
DEBAOV V. (1982) Proceedings of the IVth international symposium on
genetics of industrial microorganisms, pages 254-258, XP008031179



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The examination is being carried out on the following application documents:

Text for the Contracting States:
 DE FR GB IT

Description, pages:

1-35 as originally filed

Claims, No.:

1-5	as received on	04.08.2003	with letter of	04.08.2003
6	as received on	07.01.2004	with letter of	07.01.2004

Drawings, sheets:

1/4-4/4 as originally filed

1. **Observations** are hereby presented which take into account the communications of 2002-11-28 (C1), 2003-03-27 (C2) and 2003-09-05 (C3) and your letters dated 2003-03-11 (L1), 2003-08-04 (L2) and 2004-01-07 (L3).
2. The **amendments** introduced are in accordance with Article 123(2) EPC.
3. The following **document** (D) is cited by the examiner (see the Guidelines, C-VI, 8.9). A copy of the document is annexed to the communication and the numbering will be adhered to in the rest of the procedure:

D4: DEBABOV V.: 'Construction of strains producing L-threonine',
 PROCEEDINGS OF THE IVTH INTERNATIONAL SYMPOSIUM ON
 GENETICS OF INDUSTRIAL MICROORGANISMS, 1982, pages 254 to 258,



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XP008031179

4. NOVELTY (Art. 54 EPC)

- 4.1 D1 (cf. page 2081 left-hand column first paragraph) explicitly refers to D4 (reference number 7) and thus the teaching of the latter document may be regarded as incorporated into the document containing the reference (Guidelines, C-IV, 7.1). D1 (cf. the whole document), in combination with D4 (cf. page 257), discloses a bacterium belonging to the genus *Escherichia* (*Escherichia coli*) which has been constructed from a sucrose non-assimilative strain belonging to the genus *Escherichia*, the bacterium harboring sucrose PTS genes and having an ability to produce and accumulate an amino acid in a culture medium when the bacterium is cultivated in the medium which contains sucrose as a sole carbon source, wherein the amino acid is homoserine. Also disclosed is a method for producing said bacterium and a method for producing said amino acid using said bacterium. Thus D1, in combination with D4, anticipates the subject-matter of claims 1 and 3-6
- 4.2 Consequently, the present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1 and 3-6 is not new in the sense of Article 54(1) and (2) EPC.

5. INVENTIVE STEP (Art. 56 EPC)

- 5.1 The Examining Division maintains its inventive step objection (cf. C3 paragraphs 5.1 - 5.4).
- 5.2 Document D1 (cf. the whole document) is considered to represent the most relevant state of the art. D1 discloses a bacterium belonging to the genus *Escherichia* (*Escherichia coli*) which has been constructed from a sucrose non-assimilative strain belonging to the genus *Escherichia*, the bacterium harboring sucrose PTS genes and having an ability to produce and accumulate an amino acid in a culture medium when the bacterium is cultivated in the medium which



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contains sucrose as a sole carbon source, wherein the amino acid is tryptophan (cf. table 3). Also disclosed is a method for producing said bacterium and a method for producing said amino acid. Moreover, D1 explicitly refers to D4, which discloses a similar strategy for constructing threonine and homoserine producers.

- 5.3 According to the applicant (cf. L3 pages 3-5), D1 teaches that it is possible to produce a sucrose assimilative *E. coli* K-12 derivative, however, D1 does not teach the advantageous effect of sucrose utilization over glucose utilization. The applicant further argues that the amino acid amounts produced in a sucrose containing medium are much higher than the amounts produced in a glucose containing medium and that these unexpected results were not taught by document D1.
- 5.4 In the light of the prior art documents D1 and D4, however, it is clear that present claims 1 and 3-6 do not involve an inventive step. The applicant is reminded that the scope of the present claims comprises bacteria which produce the same amino acid amounts or less in a sucrose containing medium compared to in a glucose containing medium. Therefore, the Examining Division maintains its reasoning, as discussed in C3 paragraphs 5.4 and 5.5, that in the light of the cited prior art, it is obvious for the person skilled in the art to try, with a reasonable expectation of success, to construct other such bacteria harboring sucrose PTS genes, having an ability to produce and accumulate amino acids (e.g. homoserine, isoleucine, lysine and valine) when cultivated in a medium which contains sucrose as a sole carbon source. Moreover, the attention of the applicant is drawn to the fact that in D4 other such bacteria are already disclosed, which produce threonine and homoserine. Consequently, claims 1 and 3-6 are neither new (subject-matter relating to homoserine) nor inventive (subject-matter relating to isoleucine, lysine and valine).
- 5.5 In view of the above, the present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1 and 3-6 does not involve an inventive step in the sense of Article 56 EPC.
- 5.6 The Examining Division believes that the invention, insofar as it relates to the effect of obtaining higher yields of homoserine, isoleucine, lysine or valine using a



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medium containing sucrose instead of glucose as a sole carbon source, cannot be worked through the whole of the field claimed (see also paragraph 7). Thus, the problem of providing a bacterium which produces higher yields of homoserine, isoleucine, lysine or valine using a medium containing sucrose instead of glucose as a sole carbon source, is not solved over the whole scope of the claims 1 and 3-6 (Art. 56 EPC). It appears that an inventive step in that case can only be acknowledged for the subject-matter of claim 2, namely that the sucrose PTS genes are derived from the microorganism having the accession number VKPM B-7915, which might be responsible for the aforementioned effect.

6. NON-UNITY (Art. 82 EPC)

- 6.1 The Examining Division maintains its non-unity objection raised in C3 paragraph 5.10.
- 6.2 The application lacks unity within the meaning of Article 82 EPC. The common concept of providing a bacterium belonging to the genus *Escherichia* which has been constructed from a sucrose non-assimilative strain belonging to the genus *Escherichia*, the bacterium harboring sucrose PTS genes and having an ability to produce and accumulate an amino acid in a culture medium when the bacterium is cultivated in the medium which contains sucrose as a sole carbon source, is neither new nor inventive (see paragraphs 4 and 5).
- 6.3 Hence the Examining Division considers that bacteria relating to a different amino acid (homoserine, isoleucine, lysine and valine) constitute different solutions and thus in fact different inventions not so linked as to form a single general inventive concept in the light of D1/D4.

Since it is not clear on which invention or group of inventions the further prosecution of the application should be based, no full examination can be carried out. The applicant is asked to state upon which invention or group of inventions further prosecution of the application should be based and to limit the application accordingly. The other invention/s or group/s of inventions is/are to be excised from the claims, description and drawings if any.



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6.4 The subject-matter to be excised may be made the subject of one or more divisional applications. The divisional applications must be filed directly at the European Patent Office in Munich or its branch at The Hague and in the language of the proceedings relating to the present application, cf. Article 76(1) and Rule 4 EPC. The time limit for filing divisional applications (Rule 25(1) EPC) must be observed.

7. ARTICLES 83 AND 84 EPC

7.1 The Examining Division maintains its objections raised in C3 paragraphs 5.8 and 5.9.

7.2 The applicant still argues (cf. L3 pages 3-6) that the amino acids amounts produced in a sucrose containing medium are much higher than the amounts produced in a glucose medium and that these unexpected results were not taught by document D1. The applicant mentions that with respect to the amino acids homoserine, isoleucine, lysine and valine, the examples of the present application show that the production of amino acid using a sucrose medium is higher than the amount of tryptophan produced, thereby confirming the results obtained in document D1. Furthermore, the applicant states that as shown in tables 3 to 6, the increase in yield when using sucrose instead of glucose is from 20 to more than 50%, while in contrast thereto, in the case of tryptophan (table 7) the increase in yield is only from 12.7% to 13.7% which is about 1% (correction from L3 which states that the difference is 8%).

7.3 However, said last statement is incorrect. As shown in tables 3 to 6, the increase in yield when using sucrose instead of glucose is about 5.2%, 2.9%, 3% and 3.8% for homoserine, isoleucine, lysine and valine respectively, and not from 20 to more than 50%. The increases are thus in the same order of magnitude for homoserine, isoleucine, lysine, valine and tryptophan.

7.4 Although it is indeed shown for the specific examples of the application, i.e. specific combinations of specific amino acid producing strains harboring specific sucrose PTS genes derived from the microorganism having the accession number



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VKPM B-7915, that higher yields of homoserine, isoleucine, lysine or valine can be obtained using a medium containing sucrose instead of glucose as a sole carbon source, the Examining Division has well-founded reasons for believing that the skilled person would be unable, on the basis of the information given in the application as filed, to extend the particular teaching of the description to the whole field claimed, i.e. any bacterium belonging to the genus *Escherichia* harboring sucrose PTS genes and having an ability to produce an amino acid in a culture medium containing sucrose as a sole carbon source, using routine methods of experimentation or analysis (Art. 83 EPC). This doubt is substantiated and supported by a published document, namely D1, which discloses strains imparted to a sucrose utilizing ability which do not show an increased yield of tryptophan production when cultivated in a medium containing sucrose as a sole carbon source, compared to the yield when the microorganisms were cultivated in a medium containing glucose as a sole carbon source (Art. 84 EPC and the Guidelines, C-III, 6.3 and 6.4).

- 7.5 In the present application in the case of tryptophan (table 7) there is after all also an increase in yield from 12.7% to 13.7% which is about 1%. Thus, contrary to what the applicant states in L3 page 6, these results do not confirm the results obtained in document D1. In fact both results are completely contradictory, because D1 shows a decrease in yield while the present application shows an increase in yield. It is thus clear that an essential technical feature is missing in claim 1 which is responsible for the effect (= result to be achieved) of the present invention, that higher yields of homoserine, isoleucine, lysine, valine (and tryptophan) can be obtained using a medium containing sucrose instead of glucose as a sole carbon source. Hence, the independent claims do not meet the requirement following from Article 84 EPC taken in combination with Rules 29(1) and (3) EPC that any independent claim must contain all the technical features essential to the definition of the invention. It appears that the only distinguishing technical feature which might be responsible for the aforementioned effect is the subject-matter of claim 2, namely that the sucrose PTS genes are derived from the microorganism having the accession number VKPM B-7915. Thus, it appears that the only way of overcoming the present objections would be to incorporate the subject-matter of claim 2 into claim 1.



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7.6 Consequently, the Examining Division also believes that the invention, insofar as it relates to the effect of obtaining higher yields of homoserine, isoleucine, lysine or valine using a medium containing sucrose instead of glucose as a sole carbon source, cannot be worked through the whole of the field claimed. Thus, the problem is not solved over the whole scope of the claims 1 and 3-6 (Art. 56 EPC). It appears that an inventive step in that case can only be acknowledged for the subject-matter of claim 2, namely that the sucrose PTS genes are derived from the microorganism having the accession number VKPM B-7915, which might be responsible for the aforementioned effect.

8. CONCLUSIONS

- 8.1 The applicant is requested to file new claims which take account of the above comments. **When failing to promptly comply with the EPC requirements in the reply to this communication, summons to oral proceedings will be issued as the next official action.**
- 8.2 Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply and not be incorporated into the application (Article 123(2) EPC and the Guidelines, C-VI, 5.7 et seq.).
- 8.3 When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims. Care should be taken during revision, especially of the introductory portion and any statements of problem or advantage, not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).
- 8.4 In order to facilitate the examination of the conformity of the amended application with the requirements of Article 123(2) EPC, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based. If the applicant



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regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

- 8.5 To meet the requirements of Rule 27(1)(b) EPC, the documents D1 and D4 should be identified in the description and the relevant background art disclosed therein should be briefly discussed.

Devijver K.